REMARKS

Claims 21-27 have been canceled without prejudice, and new claims 28-32 are presented. The new claims are supported by the prior claims in this application and by the claims and Specification in PCT/GB95/00338 (WO 95/22335, filed February 17, 1995, from which priority is claimed in the present application). None of the amendments constitutes the addition of new matter.

The Effective Filing Date of Claims 1, 19 and 20

The Examiner has clarified his opinion as to priority for certain embodiments of the invention.

Applicants respectfully rebut certain statements relative to the acids disclosed in the priority documents. WO 95/22335 (filed in 1995, earlier than the Seitz priority date) is the subject of a priority claim in the present application. This priority application discloses organic acids as acidifying agents (page 3, lines 22-23), with salicylic acid and ascorbic acid disclosed as specific embodiments at page 4, lines 29-30 (and at page 3, lines 23-24), and at page 5, lines 27-28, citrate/phosphate buffer is disclosed. This should be deemed to provide an elucidation of "organic acid" and support for the genus "organic acid" as of 1995. The term organic acid is understood by those of ordinary skill in the relevant art(s). However, in the interest of advancing prosecution, Applicants have recited only those particular organic acids set forth in the 1995 priority application. The recitation of the source of nitrite ions as an alkaline metal or an alkaline earth metal nitrite is disclosed in WO 95/22335 at page 3, lines 25-26 and in the present application at page 7, lines 7-14.

Applicants respectfully rebut certain statements relative to separately disposed acidifying agent and nitrite source. WO 95/22335 provides support for separation of nitrite source and acidifying agent prior to use. Page 1 refers to oral administration of

nitrite source and acidification in the stomach via gastric acid. Page 3, lines 28-33 states that the pharmaceutically acceptable carrier or diluent may be an inert cream or ointment and that in a preferred embodiments, the acidifying agent and the source of nitrite ions or precursor thereof are "separately disposed in said cream or ointment for admixture to release nitrite ions at the environment of use". Page 4 relates to sterilization of object by mixing an acidifying agent with a source of nitrite ions in a liquid carrier or diluent in contact with the object to reduce the pH to below 4. It is clear that the inventors contemplated that it was preferred that the acidifying agent and the nitrite be mixed at the intended site of use as of the 1995 priority date, well before the effective date of the cited Seitz reference. Language related to treatment of bacterial, fungal an viral infections is found in WO 95/22335 in the Abstract and at page 2, lines 24-31, for example.

New claim 29 is supported in WO95/22335 at page 3, lines 24-26, and in the present application at page 7, lines 11.

The Rejection under 35 U.S.C. 102

Claims 21-27 have been rejected under 35 U.S.C. 102(e) as allegedly anticipated by the Seitz patent (US 6,103,275). Applicants respectfully traverse this rejection.

Seitz is said to disclose, at col. 9, lines 5-13, a 1.5% sodium nitrite gel and a separate 3.3% ascorbic acid gel, and the combination of the gels to generate NO for topical treatments.

Applicants provide the following support for a date of invention earlier than that of the filing date for the cited Seitz patent. Page 1 of WO 95/22335 refers to orally administered sources of nitrogen oxides: "Once swallowed the acid conditions of the stomach ..." and that this clearly supports the concept of separation of the nitrogenous compound and the acid." Page 2 states "The above-identified mechanism is also

applicable to the destruction of micro-organisms on the skin. For example athlete's foot or tinea pedis."

WO 95/22335 at page 2, lines 24-31, states

> We have found that nitrite at concentrations of up to 4% in an inert carrier cream or ointment when mixed with an organic acid such as salicylic acid reacts to produce oxides of nitrogen which are effective in killing infectious organisms on the skin including fungi, yeast, bacteria and viruses. The combination of nitrite and acid causes mild erythema (redness) of the skin due to release of nitric oxides but this causes no significant inflammation.

In addition, at the bottom of page 3 of the priority application WO 95/022335, it states

> The pharmaceutical acceptable carrier or diluent may be an inert cream or ointment. In a particularly preferred form of the invention the acidifying agent and the source of nitrite ions or precursor therefore are separately disposed in said cream or ointment for admixture to release nitrite ions at the environment of use.

At page 4 of WO 95/22335 it is stated

In a further aspect of the invention there is provided a method of sterilizing an object which method comprises the steps of 1) preparing a pharmaceutically acceptable acidifying agent and a pharmaceutically acceptable source of nitrite ions, 2) mixing said acidifying agent with said source of nitrite ions in a liquid carrier or diluent in contact with said object thereby to reduce the pH to below 4 while causing said sterilant nitrite ions to sterilize said object.

The Examiner has further stated that Applicant's feature of "in an amount sufficient to establish a pH at an environment of use below 4" is noted with respect to the acid component and also noted that 1-10% ascorbic acid meets that feature (claim 27, line 2). It has been stated that because Seitz discloses a 3.3 wt% ascorbic acid in a gel, this amount is sufficient to meet applicant's claim feature. Also, it is alleged that because Seitz's dosage form contains the same exact components as applicant's dosage form, the same properties must necessarily be present, "for topical treatment of a bacterial, viral or fungal infection".

With respect to the pH at an environment of use, this is taught in WO 95/22335 at page 3, lines 21-22. In the lines following 22-24, it is stated that "preferably the acidifying agent is an organic acid, for example salicylic acid or ascorbic acid." The Seitz reference appears to teach ascorbic acid and its salt and maleic acid. Clearly, the use of organic acids was set forth as of the 1995 filing date of the PCT application, prior to the filing date of the Seitz patent, even though Applicants' prior filings did not explicitly disclose certain all the current particular examples of organic acids. The art understands various particular acids that are classified generally as "organic acids" as well as the concentrations of those organic acids that would produce the noted pH of less than 4 at an environment of use. Applicants respectfully note that in addition to ascorbic and salicylic acid, the WO95/22335 priority document teaches the use of citrate in combination with phosphate buffer. See Example 4 (page 7) and Figure 4.

While the Seitz reference teaches separate gels comprising the acid and the source of nitrite ions, Applicants respectfully note that WO 95/22335 teaches creams or ointments separately containing the acidifying agent and the source of nitrite ions (See page 3, lines 28-33). This document also teaches the presentation of acid compositions in tablet or liquid form (bottom of page 3). Clearly, the use of separate compositions to be combined was contemplated prior to the filing of the Seitz patent although in a somewhat different form (cream or ointment vs. gel). In any case, claim 1 of the WO 95/22335 document recites a "dosage form", unspecified as to as an unspecified form of

therapeutic composition. Thus it sets forth a genus of dosage forms as well as a genus of organic acids. Applicants do not specifically claim a gel composition as is claimed by Seitz.

Applicants respectfully maintain that Applicants claims are entitled to a priority date earlier than the effective 102(e) date of the cited Seitz patent (in 1998). In view of the foregoing excerpts from the 1995 priority document and the amendment of the claims to be limited to the disclosure of the priority application, the rejection under 35 U.S.C. 102(e) is not proper and the rejection should be withdrawn.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended the claims to recite only those organic acids and dosage forms specifically disclosed in the 1995 priority application. Support in the present application is found, for example, at page 7, lines 10-11, and support for the recitation of alkaline earth or alkaline metal nitrite is found at page 7, lines 11-13 and in as-filed claim 12.

In view of the foregoing, Applicants respectfully maintain that the present invention as claimed is not anticipated by the cited Seitz reference, and the withdrawal of the rejection is respectfully requested.

Conclusion

Applicants respectfully submit that the pending claims are in condition for allowance and early notification thereof is requested.

If, in the interest of expediting prosecution, the Examiner has questions or comments, he is invited to telephone the undersigned at the indicated telephone number.

This Response is accompanied by a Petition for Extension of Time (three months), a Request for Continued Examination and payment of the necessary fees ($905.00 as required by 37 C.F.R. 1.17(a) and 1.17(e). It is believed that this Amendment and accompanying document does not necessitate the payment of any additional fees under 37 C.F.R. 1.16-1.17. If the amount submitted is incorrect, however, please charge any additional fees due pursuant to the foregoing Rules to Deposit Account No. 07-1969.

Respectfully submitted,

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